

CLAIMS

The invention claimed is:

1. A method of killing a mammalian cell that expresses telomerase reverse transcriptase (TERT), comprising contacting the cell with a polynucleotide in which a promoter sequence controls transcription of a transcribable sequence that is toxic to the cell or renders the cell more susceptible to toxicity of a drug;

wherein the promoter has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and contains a nucleotide sequence that is least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1.

2. A method of killing a mammalian cell that expresses telomerase reverse transcriptase (TERT), comprising contacting the cell with a polynucleotide in which a promoter sequence controls transcription of a transcribable sequence that is toxic to the cell or renders the cell more susceptible to toxicity of a drug;

wherein the promoter has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and is either

a) contained in the APAI-FSPI fragment just upstream of the encoding sequence for human telomerase reverse transcriptase (hTERT) in lambda phage GΦ5 deposited as ATCC Accession No. 98505; or

b) comprises a nucleotide sequence that hybridizes to DNA complementary to said APAI-FSPI fragment at 5 to 10°C below  $T_m$  in aqueous solution at 1 M NaCl followed by wash in  $0.2 \times \text{SSC}$ , wherein  $T_m$  is the melting temperature of the APAI-FSPI fragment in double-stranded form.

3. The method of claim 2, which hybridizes to lambda phage GΦ5 at 5°C below  $T_m$  in aqueous solution at 1 M NaCl.

4. The method of claim 2, wherein the promoter contains a nucleotide sequence that is at least 80% identical to the sequence from position -239 to position -36 from the translation initiation site of SEQ. ID NO:1.
5. The method of claim 1, wherein the promoter contains a nucleotide sequence that is at least 95% identical to the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
6. The method of claim 1, wherein the promoter contains the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
7. The method of claim 1, wherein the promoter contains the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
8. The method of claim 1, wherein the promoter is between about 400 to 900 nucleotides in length.
9. The method of claim 1, wherein the promoter is between about 200 to 400 nucleotides in length.
10. The method of claim 1, wherein the promoter is between about 100 to 200 nucleotides in length.
11. The method of claim 1, wherein the transcribable sequence encodes a protein selected from the group consisting of ricin, diphtheria toxin, other polypeptide toxins, thymidine kinase, and an enzyme that induces apoptosis.
12. The method of claim 1, wherein the drug is ganciclovir.
13. The method of claim 1, wherein the polynucleotide is an adenovirus vector.

14. The method of claim 1, wherein the cell is a cancer cell.
15. A method of treating cancer in a subject, comprising contacting cancer cells in the subject with a polynucleotide in which a promoter sequence controls transcription of a transcribable sequence that is toxic to the cell or renders the cell more susceptible to toxicity of a drug;  
wherein the promoter has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and contains a nucleotide sequence that is least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1.
16. A method of expressing a transcribable nucleotide sequence in a cell, comprising contacting the cell with a polynucleotide in which the transcribable nucleotide sequence is operably linked to a promoter sequence so as to cause it to be transcribed when the polynucleotide is in cells endogenously expressing human telomerase reverse transcriptase (hTERT)  
wherein the promoter has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and contains a nucleotide sequence that is least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1.
17. A polynucleotide in which a promoter is operably linked to a heterologous encoding region so as to cause it to be transcribed when the polynucleotide is in cells endogenously expressing human telomerase reverse transcriptase (hTERT),  
wherein the promoter contains a nucleotide sequence that is least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1.

18. A polynucleotide in which a promoter is operably linked to a heterologous sequence so as to cause the heterologous sequence to be transcribed when the polynucleotide is in cells endogenously expressing human telomerase reverse transcriptase (hTERT),  
wherein the promoter is either ✓
- a) contained in the APAI-FSPI fragment just upstream of the encoding sequence for human telomerase reverse transcriptase (hTERT) in lambda phage GΦ5 deposited as ATCC Accession No. 98505; or
- b) comprises a nucleotide sequence that hybridizes to DNA complementary to said APAI-FSPI fragment at 5 to 10°C below  $T_m$  in aqueous solution at 1 M NaCl followed by wash in  $0.2 \times \text{SSC}$ , wherein  $T_m$  is the melting temperature of the APAI-FSPI fragment in double-stranded form.
19. The polynucleotide of claim 18, which hybridizes to lambda phage GΦ5 at 5°C below  $T_m$  in aqueous solution at 1 M NaCl.
20. The polynucleotide of claim 18, wherein the promoter contains a nucleotide sequence that is at least 80% identical to the sequence from position -239 to position -36 from the translation initiation site of SEQ. ID NO:1.